DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAY 17 2000

7213 '00 MAY 18 P1:30

Diane Servello
Director, Regulatory Affairs
Andrx Pharmaceuticals, Inc.
4001 S.W. 47th Avenue
Suite 201
Fort Lauderdale, Florida 33314

Re: Docket No. 00P-0219/CP1

Dear Ms. Servello:

This responds to your citizen petition dated January 13, 2000, requesting that the Food and Drug Administration (FDA) permit the submission of an abbreviated new drug application (ANDA) for Verapamil Hydrochloride Extended-Release Tablets (once-a-day dosage), using Covera-HS[1] Extended-Release Tablets as the reference listed drug. For the reasons stated below, your request is granted.

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(j)) allows the marketing of generic versions of previously approved drug products when the generic drug product is the subject of an approved ANDA. To gain approval, the ANDA must show, among other things, that with respect to a *listed drug* (i.e., a previously approved drug product), the generic drug product has the same active ingredient in the same strength, that its labeling is essentially identical, and that it is bioequivalent. The specific approved drug product to which an ANDA refers is known as the *reference listed drug*.

FDA's policy on the designation of reference listed drugs is described in the preamble to the final rule establishing the requirements for ANDAs, published in the *Federal Register* of April 28, 1992 (57 FR 17950, 17958):

> . . . FDA will designate all reference listed drugs. Generally, the reference listed drug will be the NDA drug product for a single source drug product. For multiple source NDA drug products or multiple source drug products without an NDA, the reference listed drug generally will be the market leader as determined by FDA on the basis of commercial data. FDA recognizes that, for multiple source products, a product not designated as the listed drug and not shown bioequivalent to the listed drug may be shielded from direct generic competition. If an applicant believes that there are sound reasons for designating another drug as a reference listed drug, it should consult FDA.

[1] The sponsor for the Covera-HS application is G.D. Searle & Co.

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FDA has examined the issues presented in your petition and has determined that the grounds set forth in your petition permit designation of Covera-HS as an alternate reference listed drug under FDA policy. FDA will designate a second reference listed drug when two innovator products are bioinequivalent to each other, as is this case with Covera-HS and Isoptin SR.[2] Furthermore, the Agency has determined that it would not be in the public interest to foreclose approvals of ANDAs that wish to cite Covera-HS as the reference listed drug. Accordingly, the FDA will designate Covera-HS, in addition to Isoptin SR, as a reference listed drug in the *Approved Drug Products with Therapeutic Equivalence Evaluations* (the *Orange Book*).

FDA is aware that the presence of two reference listed drugs in the *Orange Book* may create the potential for some confusion and inappropriate substitution. FDA will take appropriate steps to make it clear in the *Orange Book* that Covera-HS and Isoptin SR are not therapeutically equivalent to each other, and that a generic drug product that is therapeutically equivalent to either Covera-HS or Isoptin SR is not therapeutically equivalent to the other.

Sincerely yours,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

[2] The sponsor for the Isoptin SR application is Knoll Pharmaceutical Co.